DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL

MINUTES OF MEETING

Immunization Practices Advisory Committee
May 10-11, 1989
Atlanta, Georgia

The Immunization Practices Advisory Committee (ACIP) met in Conference Room 207 at the Centers for Disease Control, Atlanta, Georgia, on May 10-11, 1989. Those in attendance are listed below:

COMMITTEE MEMBERS PRESENT

Dr. Samuel L. Katz, Chairman
Dr. James D. Cherry
Dr. Jeffrey P. Davis
Dr. David W. Fraser
Dr. W. Paul Glezen
Dr. Caroline B. Hall
Dr. F. Marc LaForce
Dr. H. Denman Scott
Dr. Mary E. Wilson

Ex Officio Members

Dr. John R. LaMontagne (NIH)
Dr. Paul Albrecht (FDA)

Liaison Representatives

Dr. J. Michael S. Dixon (NACI)
Dr. Susan E. Tamblyn (NACI)
Dr. Michael R. Peterson (DoD)
Dr. Stanley A. Plotkin (AAP)
Dr. William Schaffner, II (ACP)
Dr. Ronald C. Van Buren (AAFP)

Executive Secretary

Dr. Mary E. Guinan

NAVY ENVIRONMENTAL HEALTH CENTER

CDR David Trump

HHS STAFF PRESENT

CENTERS FOR DISEASE CONTROL

Office of the General Counsel

Mr. Kevin M. Malone

HHS STAFF PRESENT (continued)

CENTERS FOR DISEASE CONTROL

Epidemiology Program Office

Dr. Michael Gregg

Center for Infectious Diseases

Dr. Claire Broome
Dr. Steve Hadler
Dr. Robert Pinner
Dr. Jay Wenger

Center for Prevention Services

Dr. Roger Bernier
Dr. Steve Cochi
Ms. Rosamond Dewart
Dr. Karen Farizo
Dr. Paul Fine
Dr. Brad Hersh
Dr. Alan Hinman
Dr. Lauri Markowitz
Dr. Walter Orenstein
Dr. Peter Patriarca
Mr. George Seastrom
Dr. May Ann Sprauer
Dr. Paul Stehr-Green
Dr. Roland Sutter
Dr. Walter Williams

NATIONAL VACCINE PROGRAM OFFICE

Dr. Alan Hinman
Dr. Yuth Nimit

NATIONAL VACCINE INJURY COMPENSATION PROGRAM

Dr. Cynthia McCormick

Others Present

Mike Bronowicz
Dr. Pinya Cohen
Tony Deahl
Dr. Corry Dekker
Dino Dina
Dr. Arthur Elliott
Vicki Flick
James Froeschle
Dr. Robert Gerety
Dr. Lance Gordon
Dr. Jill Hackell
Gary Horwith
Larry Klein
Dr. Saul Krugman
Margaret Kunz
David Nalin
Dr. Lloyd Novick
Russell Neubauer
Joseph Oren
Dr. Mark Rapoport
Nancy Sabalusky
Dr. Robert L. Scott

The meeting was opened at 8:30 a.m. on May 10 by Dr. Samuel L. Katz, Chairperson. Dr. Katz introduced Dr. Susan E. Tamblyn, who will replace Dr. J. Michael S. Dixon as the Liaison Representative of the Canadian National Advisory Committee on Immunization.

Dr. Walter Dowdle, Acting Director, Centers for Disease Control (CDC), presented Dr. Jeffrey P. Davis a letter of appreciation, certificate, and CDC paperweight in recognition of his service as an ACIP member for the past 4 years. Dr. Davis' term expires June 30, 1989. Dr. Dowdle also presented a letter, certificate, and paperweight to Dr. Michael Dixon, who has represented the Canadian Committee for ACIP for over 10 years and who is retiring.

Format of ACIP Recommendations in MMWR

Dr. Michael Gregg, Acting Director, Epidemiology Program Office, requested more succinct statements be submitted by the ACIP for publication in the Morbidity and Mortality Weekly Report (MMWR). There has been a 30% increase in the length of ACIP recommendations. The average length of an MMWR article is 2.7 pages. Recommendations are becoming so long they lose major impact. There are currently over 70 articles "in the wings." Articles for publication in the MMWR are planned through August. Dr. Gregg proposed to create an "Executive Summary" of ACIP statements as a straightforward article, with basic and background information to appear in an MMWR Supplement (the name Supplement is expected to change). He would hope to implement this within the next few months as soon as extra staff are in place. Mr. Kevin Malone, Office of the General Counsel, expressed legal concern over shortening recommendations without adverse events, etc. After discussion concerning length, tables, number of documents, and timing of publication, Dr. Gregg proposed to try the two document system for 6 months. Dr. Katz proposed the hepatitis recommendation as a test, with the Supplement to be published simultaneously, with the Executive Summary in the weekly MMWR. Dr. Alan Hinman expressed concern about providing an abstract or condensed version in MMWR and suggested merely publishing the preamble in MMWR and citing the complete statement in the supplement. A vote was taken, with the majority favoring the two document system--recommendations and preamble published in the MMWR, with simultaneous publication of background information, complete recommendations, and bibliography in a Supplement.

Mumps

Dr. Paul Stehr-Green, Division of Immunization (IM), Center for Prevention Services (CPS), thanked everyone for the comments on the mumps draft. Comments have been incorporated. He distributed a revised section on disease surveillance and reporting of adverse events. The two major changes in the mumps recommendation are year of birth cohort of 1957 and exclusion as an outbreak control measure. It will be rephrased to "consider" exclusion. Dr. Jeff Davis asked how many cases constitute an outbreak of mumps. Numbers will be an onsite or local decision. Dr. Walter Orenstein, Director, IM, CPS, and Dr. Brad Hersh, IM, CPS, discussed an outbreak in Lawrence, Kansas. All of the cases were due to vaccine failure. There were 80 cases in 612 students. Age of vaccination was not a risk factor. It is recommended that people who received killed mumps vaccine should be revaccinated using live vaccine.

Measles

Dr. Walter Orenstein, IM, CPS, proposed to revise the measles vaccination policy by considering a potential 2-dose schedule. The concern is that extensive outbreak control efforts may be required forever using the current schedule of one dose of measles vaccine. Measles has not been eliminated, and we are 6 years past the target date. Obstacles are (1) inadequate coverage in inner cities, (2) measles in children younger than 15 months, and (3) vaccine failure. A single dose measles vaccination does not guarantee that measles will not be transmitted. We don't know the efficacy of a 2-dose schedule. If efficacy of the second dose equals efficacy of the first dose, there should be close to 100% efficacy for 2-dose recipients. Cost was the major reason a 2-dose schedule was not previously recommended. The real problem in school-age children was in 10-19 year olds. It would be years before results are seen if a second dose were to be implemented at school entry. The major problem in school-age populations is the inability to predict which areas will be affected by a measles outbreak. Thus, prevention of outbreaks will require efforts targeted to the entire school-age population. Therefore, ACIP should reevaluate a routine 2-dose strategy. Cost should not be a major consideration except for cost effectiveness; major research needs should be identified; and the issue of quarantine should be discussed.

The first 16 weeks of 1989 has shown a threefold increase in reported cases over the same period in 1988. If present trends continue, the number of cases reported in 1989 may be the greatest since 1980. As of the first 16 weeks of 1989, 56 outbreaks have been reported. Preschool accounts for the largest number of cases, with school-age children having the second largest number. It has been the largest college year since data have been collected. The number of deaths so far reported in 1989 is the largest number since 1977.

Dr. Orenstein distributed an agenda for measles presentations. Dr. Lauri Markowitz, IM, CPS, gave a review of information on vaccine induced immunity. Data are available from serologic and epidemiologic studies. Waning immunity has been documented in a small percentage of vaccinated persons. Questions remain as to whether revaccination of persons who have lost detectable antibody will result in lasting immunity. The eipidemiologic significance of waning immunity is also not known.

Dr. Markowitz presented epidemiologic data of efficacy of 2-dose measles vaccination schedules and data from other countries with 2-dose schedules. Although it's too early to evaluate countries with a 2-dose schedule, some epidemiologic data from outbreak investigations suggest increased protection from 2 doses of vaccine.

Dr. Markowitz, based on a variety of simplifying assumptions, compared the additional cost for a second dose to the cost of current outbreak control strategy. For a second dose of measles vaccine the cost would be $17.5 million, and for MMR the cost would be $30.7 million, assuming the second dose occurs at school entry. The cost of outbreak control using current recommendations would be $17,035,700 for measles vaccine and $27,730,400 for MMR vaccine. Outbreak control would be still necessary with a 2-dose schedule. In 15 years after the 2-dose schedule is initiated, the cost for the 2 strategies would be approximately the same.

Dr. Brad Hersh, IM, CPS, stated preliminary cost estimates in recent outbreaks based on $9.19 for measles vaccine and $16.18 for MMR vaccine. Four representative outbreaks were discussed. The costs for vaccine as part of outbreak control costs ranged from $207,000 for a college outbreak in Texas to $1.5 million for a statewide outbreak in North Carolina. A detailed summary of outbreak vaccine costs was distributed.

Dr. Lloyd Novick, Director, Center for Community Health, New York State Department of Health, presented a revised immunization policy for a 2 dose strategy in New York State. The policy will start in 1990 with 4 and 5 year olds. In addition, college entry students will be required to receive a second dose. This decision was based on two recent outbreaks. College and high schools were the major problems in which cost and control measures caused difficulty and confusion about reimmunization. New York State will administer the second dose MMR vaccine to children at kindergarten entry. This policy is expected to result in a sharp reduction in the incidence of measles and in progress toward its prevention. Increased vaccine costs are offset by the potential reduction in vaccine use during epidemics, use of medical personnel, and disruption of school and college events that occur under the current policy. There will be a public information campaign to explain the change.

Dr. Mark Rapoport, Deputy Commissioner, New York City Department of Health, presented information in favor of recommending the second dose measles immunization at 18 months of age. In New York City the problems are focused in minority populations, mainly in the preschool population. New York City has a successful program in the school age and daycare population. Dr. Rapoport estimates this strategy can increase by approximately 150% the vaccine failure cases avoided, in comparison to a 2-dose policy focusing on school entry.

Dr. Plotkin, American Academy of Pediatrics, reported on a recent Red Book meeting to decide (1) whether it's worth trying to eliminate measles-the answer was yes, and (2) to make recommendations to private practitioners. Cost would not be a governing factor. Unanimously a 2-dose schedule is recommended because of:

(1) Increasing incidence
(2) Waning immunity
(3) Primary failures
(4) Private sector cost is not as much of a burden as in the public sector
(5) Influence of State Health Officers and people from New York State.

The Committee is concerned with the lack of data on reimmunization and is not positive the second dose will work. The majority of the Committee voted for reimmunization at 6th grade. As pediatricians, they feel an exam at age 12 will be beneficial, and a second dose immunization will ensure they come in for this. Monovalent vaccine was narrowly voted for because it's cheaper, and data support its efficacy. The Red Book Committee will recommend reimmunization, regardless of the decision of ACIP, but will reconsider the age of immunization and will go along with MMR if this is what ACIP decides. They recommend age at first dose as 15 months.

Dr. Katz asked the Committee if they're in agreement on a 2-dose schedule. Dr. Davis asked if we're talking about State vs. Federal funds. Dr. Hinman stated that the Federal immunization grant budget has increased in the past and might be increased by Congress in the future. He disagreed with age 12 for the second dose. He feels school based approaches may be the best way to handle this. Dr. Orenstein added that the 2-dose schedule might be a help to secure more funding. There is a consensus that a 2-dose schedule should be recommended. Dr. Glezen recommends the first dose at 12 months of age and to immunize every child in 1991. Dr. Albrecht, FDA, discussed a study in Massachusetts that suggests immunization at 12 years of age would be best. Members tentatively agree on:

1. Every child should receive the first dose close to their first birthday.
2. Second dose should be given at school entry.
3. MMR is the vaccine of choice.
4. Second dose in older children is not precluded.

Dr. Plotkin and Dr. Markowitz will draft a recommendation to be presented to ACIP members tomorrow.

Research Priorities

Dr. Roger Bernier, IM, CPS presented the results of an exercise carried out to identify research priorities for the Division of Immunization. ACIP members and other non-CDC experts provided ratings on 26 different potential research projects. The Division will seek to carry out the highest priority projects as part of its research agenda over the next 2-3 years. The ten highest rated research needs were:

1. Edmonston-Zagreb vaccine trial in the U.S.
2. Improving vaccine coverage among inner-city preschoolers.
3. Serologic correlates of pertussis protection.
4. Rapid test for measles diagnosis.

5-8. OPV versus mixed schedule of eIPV/OPV.
Measles vaccine at 12 months of age.
Impact of a 2 dose schedule for measles vaccine.
Laboratory diagnosis of pertussis.

9-10. Risk of adverse events following vaccination.
Safety of Edmonston-Zagreb vaccine in HIV-infected children.

National Vaccine Program

Dr. Alan Hinman, Director, CPS, and Coordinator, National Vaccine Program, reported that the National Vaccine Advisory Committee met March 9-10, and the next meeting will be June 15-16. Three members to be named as replacements will be appointed for the June meeting. Ten areas for additional efforts if resources become available include pertussis, measles (implementation of a 2-dose schedule), conjugated vaccines, expanded vaccine safety studies using linked systems, vaccine evaluation units, polio (global and U.S.), hepatitis B immunization, demonstration projects on adult immunization, serological correlates of immunity, and tuberculosis control efforts. The Interagency

group has met six times since the last ACIP meeting. They have completed the draft annual report to Congress. An NPRM on vaccine information pamphlets was published in the Federal Register, and a public hearing was held. The period for public comments has been extended to August 29. The NVP Office staff will be expanded to seven, including a Deputy Coordinator and research assistant. Dr. Hinman has asked Dr. Mason to appoint a full-time coordinator.

Nine members have been named to the Advisory Commission on Childhood Vaccines. The first meeting will be later this month in Washington. Dr. Cynthia McCormick, National Vaccine Injury Compensation Program, stated this is a new program attempting to determine how to satisfy responsibilities under the Act. There have been 133 petitions for compensation thus far. Most are DTP related conditions, 10 are realted to polio, and a handful to MMR. Three have been dismissed, and 10 have been withdrawn because of cost of trial. A trust fund amounting to $100 million (to date) has been established to pay claims for injuries occuring after October 1, 1988. The fund is also being used to pay retroactive claims, but is to be reimbursed by a future appropriation. A primary review of all claims received has been conducted. Most of these claims contain inadequate data, and it may take up to 5 months to retrieve necessary data. No settlement has actually occurred yet.

Vaccine Information Pamphlets

A copy of the Federal Register Notice of Proposed Rulemaking concerning vaccine information materials being developed as a requirement of the National Childhood Vaccine Injury Act of 1986 was mailed to ACIP Members prior to the meeting. Dr. Orenstein discussed these draft information pamphlets which meet the requirements of the Act and also will serve for the "duty to warn." Vaccines covered include DTP and components, MMR and components, OPV, and IPV. The reading level is for 10-12 grade. The Notice was published March 3 with a comment period extended to August 29. A public hearing was held April 17, 1989. Approved vaccine information pamphlets will be published in the Federal Register. CDC will furnish States with camera ready copy. States will add their own material and distribute. Everyone receiving these vaccines must receive these forms and will be covered by the Vaccine Compensation Program. Grant funds will be supplemented to assist States. For reporting adverse events, there will be an attempt to have a single system with a single form (similar to FDA form). Hopefully, a contract will be awarded before October 1. Dr. Plotkin stated that these forms may retard vaccination. The same process is required for package inserts. The whole process required by law is very cumbersome.

Hepatitis

Dr. Stephen Hadler, Division of Viral Diseases (DVD), Center for Infectious Diseases (CID), discussed some of the changes in the draft recommendation for viral hepatitis. This draft was mailed to members prior to the meeting. It incorporated comments made on a previous draft distributed at the February meeting. Dr. Hadler distributed a list of major and minor issues to be discussed in connection with this draft. After some discussion of the major issues, Dr. Hadler asked members to mail their comments to him by June 15. After additional revision(s), the hepatitis recommendation will be published by this fall.

Dr. Albrecht stated that FDA approval of MSD hepatitis B vaccine is expected within the next few weeks. There are issues to be resolved with Smith Kline vaccine, and licensure will be delayed.

Polio

Dr. Stephen Cochi, IM, CPS, presented information on the status of polio eradication in the Americas. The World Health Organization (WHO) estimates that more than 250,000 cases of paralytic poliomyelitis occur each year worldwide. The introduction and widespread use of inactivated poliovirus vaccine (IPV) in 1955 and live, attenuated oral poliovirus vaccine (OPV) in 1961 had a dramatic impact on the reported incidence of poliomyelitis in the United States and other developed countries. During the early 1980s Brazil demonstrated that intensive, biannual national vaccination campaigns were very effective in substantially reducing the number of polio cases. Furthermore, the number of countries in the Western Hemisphere reporting cases decreased from 19 in 1975 to 11 in 1984. These successes led the Pan American Health Organization (PAHO) in 1985 to set the goal of regional elimination of the indigenous transmission of wild polioviruses from the Americas by the end of 1990.

Progress has been made since the goal was announced, and particularly in the two years since April 1987 when the plan of action received formal funding. In 1988, a provisional total (as of April 29, 1989) of 353 confirmed cases of polio were reported in the Region of the Americas, with 8 probable cases awaiting final classification. This provisional total represents a 62% decline from the 930 confirmed cases reported in 1986, and a 46% decline from the 656 cases reported in 1987. A steady increase in OPV coverage with 3 doses of vaccine occurred between 1980 and 1988, and reached an all-time high of 82% in 1988.

Dr. Katz requested Dr. Albrecht to convey to Dr. Paul Parkman his concern that more consistent representation from FDA would provide more effective liaison. Although Dr. Albrecht was able to be with the Committee for the first day of its meeting, he was unable to remain for the second day when Haemophilus influenza B conjugate vaccines were discussed.

Status of Vaccinia and Vaccinia Immune Globulin

Regarding information presented at the February meeting on availability of VIG, Dr. Michael Peterson, Department of Defense, reported that the Army will continue to vaccinate recruits against smallpox. The Army is pursuing vaccine stock. Dr. Ernest Takafugi, Office of the Surgeon General, HQDA, told Dr. Mary Guinan at the February meeting that the Army will try to provide VIG to CDC when necessary. Dr. Plotkin would like the Army to obtain data on encephalitis and VIG.

Meningococcal Disease

Dr. Robert Pinner, Division of Bacterial Diseases (DBD), CID, discussed recent developments in the epidemiology of meningococcal disease. He summarized the international spread of one clonal group of Group A Neisseria meningitidis, which caused epidemics in Nepal in 1983, among Hajjis (pilgrims) who traveled

to Mecca, Saudi Arabia in 1987, and in Chad in 1988. This clone was most likely introduced into the population at Mecca by South Asian pilgrims attending the Hajj; returning Hajji meningococcal carriers further disseminated this clone to their homes, with one result being the epidemic in Chad. No outbreaks of Group A disease due to this clone have occurred in the United States.

In Los Angeles, the annualized attack rate of meningococcal disease rose from 1.6 per 100,000 during the first 6 months of 1986 to 4.2 per 100,000 during the frist six months of 1987; the proportion that was Group C rose from 46% to 82%. A single electrophoretic enzyme type was responsible for most of the Group C disease in Los Angeles during 1986 and for virtually all of the increase during 1987.

This winter an outbreak of Group C meningococcal disease occurred in the area of Yakima, Washington. There were 23 cases, most of which occurred in Hispanic residents of Yakima, and 6 fatalities. Eleven of the 23 cases occurred in children 2 years of age or younger. The attack rate for Yakima County was about 10 per 100,000 population during the outbreak period, compared to an annual national incidence of 1.3 per 100,000. Contact-tracing and Rifampin prophylaxis were administered. About 15,000 people, mostly Native Americans, were vaccinated in lower Yakima County. Enzyme typing of the Yakima strains has shown that they belong to the same clonal group that was prevalent in Los Angeles in 1986.

Dr. Pinner cited these examples to show how microbiologic techniques can be used to track the spread of particular clonal groups and perhaps also to spot clones with increased virulence.

Haemophilus Influenzae

Cheryl Counts read an exchange of letters between Dr. Katz and Dr. Parkman. Dr. Katz's letter expressed ACIP support for consideration of licensure of Hib conjugate vaccines for children at 12 months of age. Dr. Parkman replied that FDA is reviewing applications for such licensure and would keep Dr. Katz informed as they progress in the decision process. Dr. Parkman also noted that FDA would require additional efficacy data before licensing a product at less than 12 months.

Dr. Jay Wenger, DBD, CID, discussed pros and cons of 12 month licensure. About 19% of Hib disease in children occurs in those from 12 through 17 months of age, and some of these cases would be prevented by licensure at 12 months of age. Problems with licensure at 12 months of age include prolongation of current efficacy trials in children less than 12 months of age, leading to delay in licensing a vaccine in infants; the need for additional physician visits; differing vaccination schedules depending on which conjugate is used; lack of efficacy data for this age group; and the possibility of an additional change in policy--dropping vaccination age to 2 months of age--within a year (if efficacy trials in children less than 12 months of age are completed). These issues were discussed by committee members.

It was decided that CDC would model the effect of different Hib conjugate licensing strategies (12 months now; wait for 2-month data) in terms of cases

of Hib disease prevented. This would include an estimate of impact of licensure at 12 months on completion dates of the prospective trials in infants. Dr. LaForce will receive modeling and forward this to ACIP members along with two ballots: (1) whether ACIP accepts serologic data as a surrogate for efficacy trials for infants 12-18 months of age, and (2) whether they would support recommending to FDA to lower the age from 18 to 12 months. Dr. LaForce will collate the results and forward them to Dr. Katz.

Measles

Drs. Markowitz, Plotkin, and Hall presented an outline of a draft measles ACIP statement (prepared the night of May 10) to members. Points mentioned in following discussion included: results from the New York proposal would be several years forthcoming; current data are needed to recommend a change in the age for routine immunization from 15 months to 12 months; the Division of Immunization has funds to do a study on the 12-15 month issue; and there is support for immunization at 12 months or younger in areas where there is a problem. Dr. Katz asked members to vote on several issues. Recommending the first immunization at 12 months instead of 15 months of age with MMR in all children was opposed. School entry age for second dose was favored over 6th grade. The Committee does not recommend quarantine. They feel the statement on routine vaccination of college students should be more specific--full-time students/part-time students/all students/students with a documented history of measles. They favor abandoning the 1980 cutoff. Two measles vaccinations is recommended for hospitals/medical facilities unless there is documented history of measles. ACIP recommends a 2-dose schedule. Dr. Markowitz will be working on a new measles recommendation.

Other ACIP Business

The date for the next ACIP meeting will be September 26-27, and the date for the first meeting in 1990 tentatively will be February 27 and 28.

With the thanks of the Chairman, the meeting was adjourned at 11:30 a.m.

I hereby certify that, to the best of my knowledge, the foregoing summary of minutes is accurate and complete.

Samuel L. Katz

Samuel L. Katz, M.D., Chairman

15 July 1989

Date